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NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	JAN 27	Source of Registration (SR) information in REGISTRY updated and searchable
NEWS	4	JAN 27	A new search aid, the Company Name Thesaurus, available in CA/CAPLUS
NEWS	5	FEB 05	German (DE) application and patent publication number format changes
NEWS	6	MAR 03	MEDLINE and LMEADLINE reloaded
NEWS	7	MAR 03	MEDLINE file segment of TOXCENTER reloaded
NEWS	8	MAR 03	FRANCEPAT now available on STN
NEWS	9	MAR 29	Pharmaceutical Substances (PS) now available on STN
NEWS	10	MAR 29	WPIFV now available on STN
NEWS	11	MAR 29	New monthly current-awareness alert (SDI) frequency in RAPRA
NEWS	12	APR 26	PROMT: New display field available
NEWS	13	APR 26	IFIPAT/IFIUDB/IFICDB: New super search and display field available
NEWS	14	APR 26	LITALERT now available on STN
NEWS	15	APR 27	NLDB: New search and display fields available
NEWS	16	May 10	PROUSDDR now available on STN
NEWS	17	May 19	PROUSDDR: One FREE connect hour, per account, in both May and June 2004
NEWS	18	May 12	EXTEND option available in structure searching
NEWS	19	May 12	Polymer links for the POLYLINK command completed in REGISTRY
NEWS	20	May 17	FRFULL now available on STN
NEWS	21	May 27	STN User Update to be held June 7 and June 8 at the SLA 2004 Conference
NEWS	22	May 27	New UPM (Update Code Maximum) field for more efficient patent SDIs in CAPLUS
NEWS	23	May 27	CAPLUS super roles and document types searchable in REGISTRY
NEWS	24	May 27	Explore APOLLIT with free connect time in June 2004
NEWS EXPRESS			MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004
NEWS HOURS			STN Operating Hours Plus Help Desk Availability
NEWS INTER			General Internet Information
NEWS LOGIN			Welcome Banner and News Items
NEWS PHONE			Direct Dial and Telecommunication Network Access to STN
NEWS WWW			CAS World Wide Web Site (general information)

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=> file medline biosis scisearch biotechno caplus

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FILE 'BIOSIS' ENTERED AT 10:32:37 ON 07 JUN 2004

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FILE 'SCISEARCH' ENTERED AT 10:32:37 ON 07 JUN 2004

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FILE 'BIOTECHNO' ENTERED AT 10:32:37 ON 07 JUN 2004

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FILE 'CAPLUS' ENTERED AT 10:32:37 ON 07 JUN 2004

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=> s lymphotoxin

L1 11251 LYMPHOTOXIN

=> s l1 and p33

L2 16 L1 AND P33

=> s l1 and beta

L3 5595 L1 AND BETA

=> s lymphotoxin-beta

L4 1441 LYMPHOTOXIN-BETA

=> s l4 and p33

L5 0 L4 AND P33

=> s l4 and hiv

L6 15 L4 AND HIV

=> dup rem l6

PROCESSING COMPLETED FOR L6

L7 9 DUP REM L6 (6 DUPLICATES REMOVED)

=> d ti 1-9

L7 ANSWER 1 OF 9 MEDLINE on STN DUPLICATE 1

TI Cytokine networks are pre-activated in T cells from HIV-infected patients on HAART and are under the control of cAMP.

L7 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN

TI Apparatus and method for flow electroporation of biological samples

L7 ANSWER 3 OF 9 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

TI Antiviral mediated suppression of NF-kappaB and induction of the EBV lytic cycle; a novel therapy for EBV-associated Burkitt's lymphoma.

L7 ANSWER 4 OF 9 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

TI Microarray analysis of brains from macaques with lentiviral encephalopathy

showed up-regulation of genes that promote virus replication and down-regulation of neurotrophic genes.

- L7 ANSWER 5 OF 9 MEDLINE on STN DUPLICATE 2  
TI Signaling through the **lymphotoxin-beta** receptor stimulates **HIV-1** replication alone and in cooperation with soluble or membrane-bound TNF-alpha.
- L7 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN  
TI Soluble **lymphotoxin-beta** receptors, anti-lymphotoxin receptor antibodies, and anti-lymphotoxin ligand antibodies as therapeutic agents for the treatment of immunological diseases
- L7 ANSWER 7 OF 9 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN  
TI Tumor necrosis factor receptor-associated factor (TRAF) 5 and TRAF2 are involved in CD30-mediated NF kappa B activation
- L7 ANSWER 8 OF 9 MEDLINE on STN  
TI TRAF5, an activator of NF-kappaB and putative signal transducer for the **lymphotoxin-beta** receptor.
- L7 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN  
TI **Lymphotoxin-.beta.** and its therapeutic uses

=> d 9 8 5 ab

- L7 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN  
AB **Lymphotoxin-.beta.** (LT- $\beta$ ), a membrane protein of lymphocytes and a number of other cell types including phorbol ester (PMA) stimulated T cell hybridoma II-23.D7 cells, is isolated and characterized and a cDNA encoding it is cloned and expressed. **Lymphotoxin-.beta.** forms complexes with other peptides such as lymphotoxin- $\alpha$  (LT- $\alpha$ ) and also forms homooligomers. The protein is involved in targeting LT- $\alpha$  to the cell surface. The LT- $\alpha$ /LT- $\beta$  complex may act as an inflammation regulating agent, a tumor growth inhibiting agent, a T cell inhibiting agent, a T cell activating agent, an autoimmune disease regulating agent, or an **HIV** inhibiting agent (no data). Furthermore, the antitumor activity of the LT- $\alpha$ /LT- $\beta$  complex may be delivered to tumor cells by tumor infiltrating lymphocytes (TILs) transfected with the gene for LT- $\beta$  (no data). LT- $\beta$  was identified as the protein with which LT- $\alpha$  was bound on the surface of T-cells. The protein was only found in B- and T-cells. Cloning of a cDNA for LT- $\beta$  by PCR using amino acid sequence-derived primers is described; the cDNA was expressed using the pCDM8 expression cassette with successful expression achieved even without the initiator AUG codon.
- L7 ANSWER 8 OF 9 MEDLINE on STN  
AB Tumor necrosis factor (TNF) receptor-associated factors (TRAFs) are signal transducers for several members of the TNF receptor superfamily. We have identified a novel member of the TRAF family by degenerate oligonucleotide polymerase chain reaction amplification that contains a zinc RING finger and zinc finger motifs, a coiled-coil region, and a C-terminal "TRAF" homology domain. In vitro translated TRAF5 binds to the cytoplasmic region of the **lymphotoxin-beta** receptor (LT-betaR) but not to several other related receptors including CD40, both TNF receptors, Fas, and nerve growth factor receptor. TRAF5 and LT-betaR coimmunoprecipitate when overexpressed in COS7 cells. TRAF5 mRNA expression is found in all visceral organs and overlaps with LT-betaR. These features distinguish TRAF5 from the other members of the TRAF family. The transcription factor NF-kappaB is activated in HEK293 cells by overexpression of full-length TRAF5 but not a truncated form lacking the zinc binding region. Furthermore, overexpression of LT-betaR in

HEK293 cells also results in activation of NF-kappaB, which is partially inhibited by the truncated TRAF5 mutant. These results show TRAF5 is functionally similar to TRAF2 in that both mediate activation NF-kappaB and implicate TRAF5 as a signal transducer for LT-betaR.

L7 ANSWER 5 OF 9 MEDLINE on STN DUPLICATE 2  
 AB The level of ongoing HIV-1 replication within an individual is critical to HIV-1 pathogenesis. Among host immune factors, the cytokine TNF-alpha has previously been shown to increase HIV-1 replication in various monocyte and T cell model systems. Here, we demonstrate that signaling through the TNF receptor family member, the **lymphotoxin-beta** (LT-beta) receptor (LT-betaR), also regulates HIV-1 replication. Furthermore, HIV-1 replication is cooperatively stimulated when the distinct LT-betaR and TNF receptor systems are simultaneously engaged by their specific ligands. Moreover, in a physiological coculture cellular assay system, we show that membrane-bound TNF-alpha and LT-alpha1beta2 act virtually identically to their soluble forms in the regulation of HIV-1 replication. Thus, cosignaling via the LT-beta and TNF-alpha receptors is probably involved in the modulation of HIV-1 replication and the subsequent determination of HIV-1 viral burden in monocytes. Intriguingly, surface expression of LT-alpha1beta2 is up-regulated on a T cell line acutely infected with HIV-1, suggesting a positive feedback loop between HIV-1 infection, LT-alpha1beta2 expression, and HIV-1 replication. Given the critical role that LT-alpha1beta2 plays in lymphoid architecture, we speculate that LT-alpha1beta2 may be involved in HIV-associated abnormalities of the lymphoid organs.

=> d 9

L7 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1994:603367 CAPLUS  
 DN 121:203367

TI **Lymphotoxin-.beta.** and its therapeutic uses  
 IN Browning, Jeffrey; Ware, Carl F.  
 PA Biogen, Inc., USA; University of California  
 SO PCT Int. Appl., 111 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9413808	A2	19940623	WO 1993-US11669	19931202
	WO 9413808	A3	19940804		
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2150249	AA	19940623	CA 1993-2150249	19931202
	AU 9460483	A1	19940704	AU 1994-60483	19931202
	AU 692146	B2	19980604		
	EP 672143	A1	19950920	EP 1994-907045	19931202
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 08507201	T2	19960806	JP 1993-514235	19931202
	US 5661004	A	19970826	US 1995-484272	19950607
	JP 2004135676	A2	20040513	JP 2003-383099	20031112
PRAI	US 1992-990304	A	19921204		
	US 1990-544862	B1	19900627		
	JP 1994-514235	A3	19931202		
	WO 1993-US11669	W	19931202		
	US 1994-222614	B1	19940401		

=> d his

(FILE 'HOME' ENTERED AT 10:32:01 ON 07 JUN 2004)

FILE 'MEDLINE, BIOSIS, SCISEARCH, BIOTECHNO, CAPLUS' ENTERED AT 10:32:37  
ON 07 JUN 2004

L1 11251 S LYMPHOTOXIN  
L2 16 S L1 AND P33  
L3 5595 S L1 AND BETA  
L4 1441 S LYMPHOTOXIN-BETA  
L5 0 S L4 AND P33  
L6 15 S L4 AND HIV  
L7 9 DUP REM L6 (6 DUPLICATES REMOVED)

=> dup rem l2

PROCESSING COMPLETED FOR L2

L8 4 DUP REM L2 (12 DUPLICATES REMOVED)

=> d 1-4 ab

L8 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN

AB The title complex is disclosed. These proteins are found on the surface of a number of cells, including phorbol ester-stimulated T-cell-hybridoma II-23.07 cells. The proteins and complexes are useful as antiinflammatory agents, T-cell activating agents, tumor growth-inhibiting agents, and enhancers of tumor infiltrating lymphocytes; they may also be used in the treatment of human immunodeficiency virus infection. **Lymphotoxin** and the associated **p33** protein were purified from phorbol myristoyl acetate-stimulated II-23.07 cells. The amino-terminal sequence(s) for **p33** is reported; the amino acid sequence of the membrane-associated **lymphotoxin** band exactly matched that described for secreted **lymphotoxin**. The functional relevance of total tumor necrosis factor or **lymphotoxin** to T-cell activation is described.

L8 ANSWER 2 OF 4 MEDLINE on STN DUPLICATE 1

AB The expression of membrane-associated forms of **lymphotoxin** (LT) and TNF were examined on cell lines of T, B, and myeloid origin, IL-2 dependent T cell clones, and peripheral blood lymphocytes. Inducible and constitutive patterns of surface LT expression were found on T cells as exemplified by the II-23.D7, a CD4+T cell hybridoma, and HUT-78, a T cell lymphoma. Phorbol ester induced surface LT expression on Ramos, an EBV transformed B cell line, but at a slower rate of appearance when compared to the II-23.D7. Secretion of LT was rapidly inducible by phorbol ester in II-23.D7 and also in HUT-78 but with slower kinetics; surface LT expression continued in both lines after secretion had ceased. Low levels of membrane TNF were transiently induced on II-23.D7 and HUT-78, but none was observed on Ramos. Peripheral blood monocytes and some myeloid tumor lines did not express surface LT. Several T cell clones expressed surface LT after Ag-specific stimulation, and expression persisted several days. Stimulation through the TCR or by IL-2 rapidly induced surface LT on resting peripheral T cells and CD56+ NK cells; pokeweed mitogen activation induced expression on CD20+ B cells. Consistent with previous results, immunoprecipitation with anti-LT mAb showed that LT was complexed with a distinct 33 kDa glycoprotein (**p33**) on cells that expressed surface LT, whereas secreted LT was not associated with **p33**. Surface and secreted modes of LT expression by activated T, B, and NK cells suggests that LT can be utilized as either a localized or diffusible mediator in immune responses.

L8 ANSWER 3 OF 4 MEDLINE on STN DUPLICATE 2

AB We characterized the membrane-associated form of **lymphotoxin** (surface LT) on the activated II-23.D7 T cell hybridoma. Antibodies to rLT precipitated both surface LT and a distinct 33-kDa glycoprotein (**p33**). Because **p33** and surface LT were antigenically

unrelated, their coprecipitation suggested a physical association of p33 and surface LT on the membrane. Pulse-chase analysis indicated that LT and p33 associate with each other early in the LT biosynthetic pathway, precluding the possibility that LT is secreted and bound to p33 or a surface receptor. Furthermore, no p33 was associated with the secreted form of LT. Isoelectric focusing of surface LT and p33 under nondenaturing and denaturing conditions confirmed that surface LT and p33 existed as a complex. Treatment of cells with a high concentration of salt or with acid indicated that surface LT is a peripheral membrane protein. Although secreted LT is a homologous trimer, protein cross-linking studies revealed that surface LT existed as a monomer associated with a dimer of p33. Together the results demonstrate a novel mechanism for stable membrane expression of LT by activated T cells.

L8 ANSWER 4 OF 4 MEDLINE on STN DUPLICATE 3  
 AB A human T cell hybridoma, II-23.D7, was induced with phorbol ester to express a surface form of **lymphotoxin** (LT, TNF-beta) and an associated 33-kDa glycoprotein. The LT epitopes were detected by surface immunofluorescence staining and by immunoprecipitation from radioiodinated or biosynthetically labeled cells with the use of anti-rLT polyclonal and monoclonal antibodies. The epitopes detected by the antibody were related to LT because adsorption of the anti-rLT with PMA-activated II-23.D7 cells resulted in the removal of the neutralizing titer of the anti-rLT antiserum. Immunoprecipitation of surface radioiodinated II-23.D7 cells revealed two bands of 25 kDa and 33 kDa that were specifically precipitated with anti-rLT, but not anti-rTNF antibodies. Enzymatic digestion with glycanases showed both proteins to have N-linked carbohydrate, with O-linked sugar limited to the 25-kDa protein. To determine the biochemical relationship between these proteins, the two LT-like forms were purified from detergent-solubilized II-23.D7 cells by immunoaffinity chromatography. Peptide mapping using CNBr cleavage showed the 25-kDa surface form to be identical to rLT, whereas the 33-kDa protein was different. Biosynthetic labeling studies showed that p33 contained both methionine and cysteine, whereas the p25 contained only methionine. Thus, the surface LT form lacks a leader peptide indicating an anchoring mechanism distinct from that described for membrane TNF. The nature of the attachment of this LT form to the membrane surface is not clear, however, neither TNF receptor binding nor lipid linkages appear to be involved. The accessory protein, p33, may anchor LT to the surface. These findings identify a new characteristic of LT and point toward an additional pathway by which T lymphocytes may mediate cytolytic activity and regulate inflammatory processes.

=> d 2

L8 ANSWER 2 OF 4 MEDLINE on STN DUPLICATE 1  
 AN 93094581 MEDLINE  
 DN PubMed ID: 1281193  
 TI Expression of surface **lymphotoxin** and tumor necrosis factor on activated T, B, and natural killer cells.  
 AU Ware C F; Crowe P D; Grayson M H; Androlewicz M J; Browning J L  
 CS Division of Biomedical Sciences, University of California, Riverside 92521-0121.  
 NC DK-07310 (NIDDK)  
 SO Journal of immunology (Baltimore, Md. : 1950), (1992 Dec 15) 149 (12) 3881-8.  
 Journal code: 2985117R. ISSN: 0022-1767.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Abridged Index Medicus Journals; Priority Journals  
 EM 199301

ED Entered STN: 19930129  
Last Updated on STN: 19960129  
Entered Medline: 19930114

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FILE CONTAINS CURRENT INFORMATION.  
LAST RELOADED: Jun 4, 2004 (20040604/UP).

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FILE 'MEDLINE, BIOSIS, SCISEARCH, BIOTECHNO, CAPLUS' ENTERED AT 10:32:37  
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L1	11251 S LYMPHOTOXIN
L2	16 S L1 AND P33
L3	5595 S L1 AND BETA
L4	1441 S LYMPHOTOXIN-BETA
L5	0 S L4 AND P33
L6	15 S L4 AND HIV
L7	9 DUP REM L6 (6 DUPLICATES REMOVED)
L8	4 DUP REM L2 (12 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 10:42:27 ON 07 JUN 2004

=> s l4 and immun?

	0 LYMPHOTOXIN
	0 BETA
	0 LYMPHOTOXIN-BETA
	(LYMPHOTOXIN(W) BETA)
	15 IMMUN?
L9	0 L4 AND IMMUN?

=> s l4 and neoplasm

	0 LYMPHOTOXIN
	0 BETA
	0 LYMPHOTOXIN-BETA
	(LYMPHOTOXIN(W) BETA)
	0 NEOPLASM
L10	0 L4 AND NEOPLASM

=> s l4 and lupus

	0 LYMPHOTOXIN
	0 BETA
	0 LYMPHOTOXIN-BETA
	(LYMPHOTOXIN(W) BETA)
	0 LUPUS
L11	0 L4 AND LUPUS

=> s l4 and diabetes

0 LYMPHOTOXIN  
0 BETA  
0 LYMPHOTOXIN-BETA  
    (LYMPHOTOXIN(W) BETA)  
1 DIABETES  
0 L4 AND DIABETES

L12

## WEST Search History

DATE: Monday, June 07, 2004

<u>Hide?</u>	<u>Set Name</u>	<u>Query</u>	<u>Hit Count</u>
<i>DB=USPT; PLUR=YES; OP=ADJ</i>			
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<input type="checkbox"/>	L7	l4 or l5	14
<input type="checkbox"/>	L6	l4 or l5L5	17
<input type="checkbox"/>	L5	p33 and l2	7
<input type="checkbox"/>	L4	p33 and L3	14
<input type="checkbox"/>	L3	L1 and immun\$	1178
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<input type="checkbox"/>	L1	lymphotoxin	1205

END OF SEARCH HISTORY